cidal action on *S. pallida in vitro*. This observation has been generally accepted, and the mechanism whereby the drug exerts its therapeutic action in syphilis has been a problem of long standing. It is usually assumed that its therapeutic effect rests on its conversion *in vivo* to some other actively spirocheticidal substance.

Contrary to this general impression, we have found that arsphenamine, neoarsphenamine, silver arsphenamine and "arsenoxide" (metaminoparhydrooxyphenylarsenoxide) effect a complete immobilization *in vitro* of virulent *S. pallida* (Nichols strain) obtained from rabbit testicular chancres. Moreover, these immobilized organisms are non-infectious for rabbits, as shown both by testicular inoculation and by subsequent lymph node transfer, and are presumably dead.

The rate at which this antispirochetal action proceeds, and the minimal effective concentration of the arsenical, depend on numerous variables. Thus, there is a large positive temperature coefficient in the range 23° to 37° C. Serum, tissue particles and, in particular, a tissue mash, all *inhibit* the antispirochetal effect, perhaps because they combine with the arsphenamines. The degree of aerobiasis seems to have but little effect.

Under appropriate experimental conditions, arsphenamine and neoarsphenamine have a definite spirocheticidal effect *in vitro* within eight hours in at least 1:250,000 dilution; and "arsenoxide" immobilizes the organisms in dilutions of at least one million. It is of interest that these concentrations are of the same order of magnitude as those attained *in vivo* after the therapeutic administration of these drugs.

Experiments are now in progress to ascertain to what extent oxidation products of the arsphenamines, formed under the conditions of the experiment, contribute to their antispirochetal action. It is further obvious that *in vitro* results have no necessary implication with respect to the therapeutic action of the arsphenamines *in vivo*. Nevertheless, the current concept that the arsphenamines are converted only *in vivo* to a directly spirocheticidal agent is based on their supposed inactivity when added to the organisms *in vitro*. Since that initial premise is apparently in error, it becomes advisable to reinvestigate the possibility, first, that the therapeutic action of the arsphenamines may rest in part on a spirocheticidal effect similar to that observed *in vitro*, and second, that this spirocheticidal action may be an intrinsic property of the arsphenamines *per se*, rather than of degradation products liberated *in vitro* or *in vivo*. Although the arsphenamines are undoubtedly converted to other substances *in vivo* in the course of their elimination, such conversion may perhaps not be an essential preliminary to their therapeutic action.

Several other implications of possible practical importance may be pointed out. As will be described in a following paper, the immobilizing activity of a given arsenical can be assayed by a simple *in vitro* experiment. It becomes of interest to ascertain the degree of correlation between antispirochetal activity as determined by this *in vitro* test, and therapeutic activity as determined in infected rabbits. Finally, the *in vitro* technique should facilitate the study of the chemical nature of the reaction between arsphenamines and spirochetes, and the development of new therapeutic agents with more favorable therapeutic: toxic ratios. Work along these several lines of investigation is now in progress.

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## A RELATION BETWEEN THE AVERAGE MASS OF THE FIXED STARS AND THE COSMIC CONSTANTS

THE physics of the universe is essentially characterized by the three following relations which are fulfilled as to the order of magnitude:[1]

$$(1)\quad N = (R/a)^2$$
$$(2)\quad T = 1/u$$
$$(3)\quad R/a = e^2/(f\, m_p\, m)$$

R and T being the radius and the age of the universe, N the total number of protons and neutrons, u Hubble's constant (500 km/sec. per mega-parsec. $= 1.6 \times 10^{-17}$ sec.$^{-1}$), f Newton's gravitational constant, e the fundamental charge, $m_p$ and m the masses of the proton and the electron, respectively, and a the classical radius of the electron $(e^2/(mc^2))$.

A further relation might be added to the above three connecting M, the average mass of a fixed star, with the cosmical constants. It has the simple form

$$(4)\quad f\, M^2 = N\, e^2.$$

If we assume that equations (3) and (4) are fulfilled not only as to the order of magnitude, but exactly,[2] we arrive at a remarkable result. Dividing equation (4) by equation (1) written in the form

$$R^2 = N\, a^2,$$

we find

$$(5)\quad (f\, M^2)/R^2 = e^2/a^2.$$

According to this formula the gravitational force which two fixed stars of average mass exert upon each other, at a distance equal to the radius of the universe, is as large as the electrostatic force acting between two fundamental charges at a distance equal to the classical radius of the electron.

[1] *Cf.* P. Jordan, *Naturwiss.*, 25: 513, 1937; A. Haas, *Naturwiss.*, 25: 733, 1937.

[2] *Cf. Physical Review*, 53: 207, 1938, Abstract of the Chicago meeting of the American Physical Society, No. 25.

If in equation (4) we insert that value for N which results from a combination of equations (1) and (3), that is

$$(6)\quad N = e^4/(f^2 m_p^2 m^2)$$

we find

$$(7)\quad M = e^3/(f^{3/2} m_p m).$$

By inserting on the right-hand side of (7) the well-known values for the constants, we obtain

$$(8)\quad M = 4 \times 10^{33} \text{ grams}$$

or about twice the mass of the sun. This result is in good agreement with astronomical observations, since the fixed stars were found to have masses varying between about 0.2 and 50 times the mass of the sun, the average mass being a modest multiple of that of the sun.

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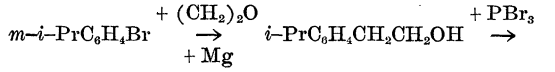
## AN APPROACH TO THE SYNTHESIS OF FICHTELITE

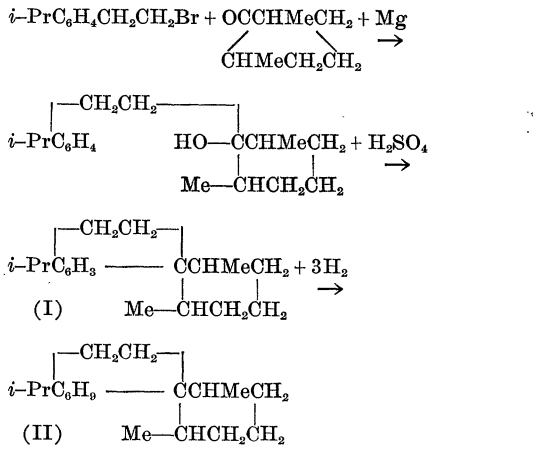
ONE of the most interesting of the retene derivatives is the fichtelite which occurs, usually associated with retene itself, in partially fossilized pine trunks found in various European peat and lignite beds. Its source is evidently the resin acids originally present in the coniferous woods in which it lies buried. It has been known for just about a century. For many years it was believed to be perhydroretene, $C_{18}H_{32}$, until Ipatiew's synthesis of the latter proved that the two were not identical. Based upon some new experimental work, Ruzicka and Waldmann recently[1] proposed for fichtelite the structure of 12-methyl-perhydroretene, or perhydroabietane, $C_{19}H_{34}$ (II).

In the January, 1938, issue of the *Journal* of the American Chemical Society, Fieser and Campbell (p. 167) have described a tetrahydroabietic acid (m.p. 163–164.5°), decarboxylation of which should yield 12-methyl-perhydroretene.

Since in these laboratories we have for some time been attacking, from the synthetic side, this problem of the constitution of fichtelite, it seems to us desirable to report here briefly the progress to date.

Steps followed in this synthesis have been the following, using *m*-bromocumene as the initial material:




The octahydro derivative (I) gave retene when fused with selenium. Catalytically hydrogenated at 225° and 150 atmospheres pressure, for four hours, in the presence of Raney nickel, in methylcyclohexane solution, it absorbed 3 moles of hydrogen per mole of hydrocarbon, with formation of a $C_{19}H_{34}$ hydrocarbon, as an odorless, colorless, transparent, viscous oil, b.p. 179–181° at 12 mm., $n_{25}^{D}$ 1.5025, which congealed to a glassy solid when cooled well below laboratory temperature. With cold alkaline permanganate or with a carbon tetrachloride solution of bromine, it behaved as a saturated compound and also was inert to concentrated sulfuric acid.

As fichtelite is a white crystalline solid, m.p. 46°, our synthetic product obviously is not identical therewith. It may be that the difference between the two is a stereochemical one[2] or that our product requires further purification.

A critical comparison of the synthetic with the natural product has been delayed by the difficulty we have encountered in securing an adequate supply of fichtelite.

The research is being continued, in the endeavor to clear up these points.

To Professor Homer Adkins, of the University of Wisconsin, we are particularly indebted for his assistance in the catalytic hydrogenation of the octahydro derivative (I).

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# SCIENTIFIC APPARATUS AND LABORATORY METHODS

## A BATH FOR SMOOTH MUSCLE

IT is difficult when recording smooth muscle contractions *in vitro* to change the fluid surrounding the muscle without exposure of the preparation to the atmosphere. This may be accomplished rapidly and easily with the smooth muscle bath shown in the ac-

[1] *Helv. Chim. Acta*, 18: 611, 1935.

[2] *Cf.* Ruzicka, Balaš and Schinz; *Helv. Chim. Acta*, 6: 695, 1923.